Drug Information Bulletin

Drug Information Centre (DIC)

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Content

Editorial

Recent controversy regarding fixing of price of medicines not included in the National Essential Medicines List 2011 (NLEM 2011) is a whistleblower to the policy makers. NPPA exerted its power as per the provision of Paragraph 19 of DPCO 2013, which authorizes the NPPA "in extraordinary circumstances, if it considers necessary so to do in public interest, fix the ceiling price or retail price of any drug for such period as it deems fit". Some industrial organizations went to the court with an appeal that NPPA wrongly utilized this provision.

This situation cropped up due to the several reasons-

Firstly the EML which was prepared in the year of 2011 is not updated, as a result some other strength or dosage form of the existing medicines left out. Some more drugs showed more efficacy over the existing medicines and being prescribed by the doctors frequently are not included in the existing EML.

Secondly it is a tendency of a sector of manufacturers to manufacture and promote medicines in the strength & dosage form not been included in the existing EML to avoid price control. This situation can be avoided by regular updating the NLEM like WHO, who updated the list every two years and strict enforcement of EML. Judicious approval of new strength and dosage form of the medicines already included in the existing EML and restricting aggressive marketing of medicines having no or least therapeutic advantage could be an effective measure.

Government of India has already started to adopt the above measures-as per reliable sources.

Dr. Subhash C. Mandal
Editor

IPA Bengal Branch received prestigious "Best Branch Award" for fourth time

IPA Bengal branch has won the "Best Branch Award" for the year 2013. Earlier this branch has made hat trick by winning the same award in the year of 2006, 2007 & 2008. This branch also won "Special Achievement Award" in the year of 2004 and 2012.

IPA used to recognize one of the 22 State branches spreading the entire country for their outstanding activities every year.

IPA Bengal Branch team receiving Best Branch Award from Dr. Rao Vadlamudi – President, IPA

Dr. Subhash C. Mandal sharing his views during Award Ceremony

IPA office bearers during Award ceremony

New Drug: Afatinib

Approved indication: non-small cell lung carcinoma

Giotrif (Boehringer Ingelheim)

10 mg, 30 mg, 40 mg and 50 mg film-coated tablets

Australian Medicines Handbook section 14.2.3

Like erlotinib (Aust Prescr 2006;29:53-5), gefitinib (Aust Prescr 2003;26:94-5) and crizotinib (Aust Prescr, published online 2014 Apr 16), afatinib is a tyrosine kinase inhibitor approved for advanced or metastatic non-small cell lung carcinoma. Afatinib irreversibly binds to the ErbB family of epidermal growth factor receptors – ErbB1 (epidermal growth factor receptor or EGFR), ErbB2 (human epidermal growth factor receptor 2 or HER2), ErbB3 and ErbB4. By blocking signalling from these molecules, afatinib slows down the growth and spread of tumour cells.

About 10% of Australian patients with non-small cell lung carcinoma have mutations in the EGFR gene. These are activating mutations which contribute to the malignant phenotype – the two most common are Del 19 (deletion in exon 19) and L858R (point mutation in exon 21). Afatinib is only approved for patients who have tumours with these mutations.

An open-label phase III comparative trial assessed the efficacy of afatinib (40 mg once a day) as a first-line treatment in 345 patients with an activating mutation in their EGFR gene. A subgroup of 308 patients had the Del 19 or L858R mutation. After a median of 11 months, afatinib significantly prolonged median progression-free survival compared to chemotherapy. In the afatinib group, progression-free survival was 2.5 months longer in those with Del 19 or L858R mutations. Afatinib did not significantly prolong overall survival compared to chemotherapy.1

Efficacy of afatinib in advanced non-small cell lung carcinoma

In a questionnaire about symptoms, the onset of cough (p=0.007) and dyspnoea (p=0.015) was significantly delayed with afatinib compared to chemotherapy. However, diarrhoea, dysphagia and sore mouth were reported to be worse.2

A phase II trial in lung adenocarcinoma found that median progression-free survival was slightly longer for patients who received afatinib first-line compared to those who received afatinib after chemotherapy had failed (see Table).3 In a subgroup of 23 patients who did not have the Del 19 or L858R mutation, median progression-free survival was only 3.7 months.3

In a trial of 62 patients who had become resistant to previous treatment with erlotinib,

gefitinib or both, response to afatinib treatment was poor (5 partial responses). Mean treatment duration was 4.6 months and median progression-free survival was 4.4 months.4

Adverse reactions to afatinib were very common with approximately half of the participants having at least one serious adverse event (grade 3 or more). Rash (16.2% of people), diarrhoea (14.4%), paronychia (11.4%) and stomatitis/mucositis (8.7%) were the most common serious events.1

Almost everyone who takes afatinib develops diarrhoea so it is important to warn patients of this. Pre-emptive antidiarrhoeal drugs, such as loperamide, can be prescribed and should be started as soon as symptoms occur. Monitoring of serum electrolytes may be needed depending on the severity and duration of diarrhoea, and the afatinib dose may need to be reduced, interrupted or stopped. Dose changes should also be considered for severe skin reactions, such as bullous, blistering and exfoliative skin conditions.

Interstitial lung disease has been reported with afatinib and has been fatal in some cases. Sudden onset or worsening dyspnoea, cough or fever should be investigated and treatment stopped if it is diagnosed. Severe hepatic impairment has also been reported so regular monitoring of liver function is recommended.

Referral to an ophthalmologist should be considered for patients who develop eye symptoms such as inflammation, lacrimation, blurred vision, light sensitivity or pain, as ulcerative keratitis can occur. Contact lenses increase the risk of these adverse events.

Inhibitors of HER2 have been associated with left ventricular dysfunction so cardiac monitoring should be considered in patients who have risk factors.

Women of childbearing age should avoid becoming pregnant while taking afatinib as it has the potential to cause fetal harm. In animal studies, afatinib was excreted in breast milk so breastfeeding is not recommended.

Following oral administration, peak plasma concentrations of afatinib are reached within 2−5 hours. The terminal half-life is 37 hours with the dose being excreted in the faeces (85%) and urine (4%). Exposure to afatinib is increased in women, those with a low body weight and those with renal impairment so closer monitoring for adverse effects is recommended for these patients. Afatinib is not recommended if renal or hepatic impairment is severe.

Drug exposure is decreased when afatinib is taken with a high-fat meal so food should be avoided for at least three hours before and one hour after taking a dose. The recommended starting dose of 40 mg a day can be escalated to 50 mg a day. However, there is no extra proven benefit at this dose and adverse events are more common.3

Afatinib is a substrate for P-glycoprotein so strong inhibitors and inducers of this transporter may affect plasma concentrations. Strong inhibitors (such as ketoconazole, erythromycin and verapamil) should only be administered at the same time or after the afatinib dose.

Afatinib adds to the treatment options for patients with non-small cell lung cancer, but patients must have the Del 19 or L858R mutation to qualify for treatment. Afatinib slows disease progression when used first-line or after chemotherapy, but showed little benefit in patients who had previously been treated with erlotinib or gefitinib. As with other drugs in this class, severe, and sometimes fatal, adverse reactions to afatinib can occur and often limit treatment.

References:

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lung adenocarcinoma with EGFR mutations. J Clin Oncol 2013;31:3327-34.
2. Yang JC, Hirsh V, Schuler M, Yamamoto N, O'Byrne KJ, Mok TS, et al. Symptom control and quality of life in LUX- Lung 3: a phase III study of afatinib or cisplatin/pemetrexed in patients with advanced lung adenocarcinoma with EGFR mutations. J Clin Oncol 2013;31:3342-50.
3. Yang JC, Shih JY, Su WC, Hsia TC, Tsai CM, Ou SH, et al. Afatinib for patients with lung adenocarcinoma and epidermal growth factor receptor mutations (LUX-Lung 2): a phase 2 trial. Lancet Oncol 2012;13:539-48.
4. Katakami N, Atagi S, Goto K, Hida T, Horai T, Inoue A, et al. LUX-Lung 4: a phase II trial of afatinib in patients with advanced non-small-cell lung cancer who progressed during prior treatment with erlotinib, gefitinib, or both. J Clin Oncol 2013; 31:3335-41.

Source: Aust Prescr 2014;37:139-43

NHRC notice to Odisha Government on Expired Medicines

The National Human Rights Commission (NHRC) has sought an action-taken report from Odisha government on the reports that low-quality and time-expired medicines were administered to patients in the state, a petitioner said Wednesday.

In response to a petition filed by Odisha-based human rights campaigner Akhand last month, the commission has ordered the principal secretary of the health ministry to file a report within four weeks, Akhand told this reporter.

On the basis of the report of Comptroller and Auditor General (CAG) of India, tabled in the state assembly last month, the petitioner alleged that 31 types of time-expired medicines were administered to patients in the state 2007-13.

According to the CAG report on the state's general and social sector for the year ended March 2013, time-expired medicines valued at Rs.74,000 were administered to patients in Cuttack, Jajpur, Mayurbhanj and Sundergarh districts during 2007-13.

The CAG report also said that during audit, it found that 19 essential drugs valued at Rs. 14.84 lakh procured during 2008-09 were distributed to various rural medical institutions without any quality testing, and administered to rural patients.

Akhand said the use of time-expired and low-quality medicines may cause allergic or toxic reactions.

He had sought intervention of the NHRC saying that the state government was reluctant to probe the matter.

Forthcoming Events

2014
IPA / EDQM
4th Technical workshop
Venue: Hotel Lalit, Sahar Road, Mumbai
Theme: Quality of Pharmaceutical Ingradients-Applying Learning to Practice
Date: 9th – 10th September 2014
For details:
http://www.ipapharma.org/events/E-Brochure-09%20(1).pdf

2nd National Pharmacists Day Celebration
25th September 2014

Organized by:
IPA Bengal Branch

- Public Awareness programme "KYM"
- Wishing recovery to Hospital Patients
- Seminar on "Antibiotic Resistance"

Platinum Jubilee Celebration of IPA cum NPW celebration
15th – 23rd November 2014

Organized by: IPA Bengal Branch
Inauguration: 15th November 2014
Workshop: 16th November 2014
Different programmes throughout the week